

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/013049

International filing date (day/month/year)
17.11.2004

Priority date (day/month/year)
17.11.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/82, C07K14/435, C12N15/11, C12N15/63

Applicant
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/EP2004/013049

AP20 Rec'd PCT/PTO 16 MAY 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☒ contained in the international application as filed.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/013049

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-5,8,11,18,19,23-26
	No: Claims	1,6,7,9,10,12-17,20-22
Inventive step (IS)	Yes: Claims	
	No: Claims	2-5,8,11,18,19,23-26
Industrial applicability (IA)	Yes: Claims	1-26
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.
AP20 Rec'd PCT/PTO 16 MAY 2006
 PCT/EP2004/013049

Present application provides means to silence insect genes by using unpackaged dsRNA; according to the present application unpackaged dsRNA or siRNA can be used to obtain gene silencing in insects through feeding. In a preferred embodiment, the feeding is on a plant which expresses the dsRNA or siRNA so that it enters the sap contained in its vascular system. Thereby said dsRNA or siRNA is not contained in a cell or transfecting promoting agent. Chimeric genes, plants comprising stably inserted said chimeric genes in their genome, phloem and phloem sap of said plants as well as methods to silence a gene in a plant-sucking insect, methods of identifying gene function in a sap-sucking insect and methods of identification of novel targets for insecticidal compounds are claimed.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The following documents were taken into account:

- D1: WO 01/37654 A (DNA PLANT TECHNOLOGY CORPORATION; TOBIAS, CHRISTIAN; SHAH, GOWRI; GUTT) 31 May 2001 (2001-05-31)
- D2: DATABASE EMBL M.persicae ecdysone receptor 11 October 1999 (1999-10-11), XP002317945 retrieved from EBI Database accession no. AAX90669
- D3: WO 01/34815 A (CAMBRIA BIOSCIENCES, LLC) 17 May 2001 (2001-05-17)
- D4: WO 03/076619 A (COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION) 18 September 2003 (2003-09-18)
- D5: WO 03/004644 A (COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION; WHYARD,) 16 January 2003 (2003-01-16)
- D6: CA-A1-2 094 658 (ALLELIX BIOPHARMACEUTICALS INC) 24 October 1993 (1993-10-24)

V.2 Novelty (Article 33(2) PCT)

- 2.1 D1 discloses a method for conferring parasitic nematode and insect pest resistance to plants by expressing in a plant a dsRNA having substantial sequence identity to an endogenous gene of the nematode or insect. Said dsRNA is taken up by insects, such as sap-sucking insects, by feeding via their sucking mechanism. dsRNA comprising 25 - 100 base pairs, plant-expressible promoters, constitutive and specific promoters (e.g phloem specific promoters) as well as essential genes are referred to (page 2, line 33 - page 4, line 32; page 7, lines 17 - 33; page 18, lines 14 - 17; page

21, line 14 - page 22, line 19; Example 8; claims 1, 6, 32 and 35). Hence, D1 appears to anticipate the subject-matter of claims 1, 6, 7, 9, 10, 12 - 17, 20 and 21. Said claims are therefore objected under Article 33(2) PCT.

- 2.2 D2 discloses a sequence showing 100% identity in 408 nt overlap with SEQ ID NO:11 (247-654:1-408). D2 is therefore prejudicial to the novelty of claim 22 and said claim does not fulfill the requirements of Article 33(2) PCT.

V.3 Inventive Step (Article 33(3) PCT)

- 3.1 The dependent claims 2 - 5, 8 and 11 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:
Said claims refer to different (essential) genes/sequences and to different promoters. However, essential genes of sap-sucking insects and the deleterious effect of the inhibition of said genes by the expression of dsRNA are well disclosed in the prior art (e.g. D3: Abstract, page 21, paragraph 1; D4: page 32, line 17 - page 33, line 6). In addition, different plant-specific promoters are described in the prior art and it is of general knowledge that different vascular and phloem-specific promoter can be used in order to direct gene expression in said parts of a plant. Hence, an inventive step cannot be acknowledged for claims 2 - 5, 8 and 11 (Article 33(3) PCT).
- 3.2 Claims 18 and 19 are directed to methods of identifying gene functions in sap-sucking insects and to method of identification of novel targets for insecticidal compounds. With regard to the disclosure of D3 (page 5, paragraph 4 - page 7, paragraph 3) said methods are obvious and straight forward for a person skilled in the art. Hence, claims 18 and 19 appear to lack inventive step (Article 33(3) PCT).
- 3.3 D5, which is considered to represent the closest prior art for evaluating the inventiveness of the subject-matter referred to in claims 23 - 26, concerns gene silencing in arthropods using dsRNA. DsRNA is delivered by a process comprising feeding the dsRNA to the arthropod or by contacting the arthropod with the dsRNA whereby reference to the use of different transfection-promoting agents, in particular to cationic lipid containing compounds, is given (page 6, lines 4 - 23; page 13, line 16 - page 20, line 12; Tables 5 - 7).

The present application differs from D5 in that a cationic oligopeptide such as a poly-Arginine peptide is used.

The problem to be solved by the present application is the provision of an alternative method of applying naked dsRNA to a plant-sucking insect.

D6 already refers to the use of carrier peptides consisting of 8 - 10 arginine residues to deliver agents such as polynucleotides to an intracellular environment (claims 1, 2, 7 and 8). It would be obvious for the person skilled in the art to combine the teaching of D5 with the disclosure of D6. Hence, claims 23 and 24 as well as the subject-matter referred to in claims 25 and 26 appears to lack inventive step (Article 33(3) PCT).

V.4 Industrial Applicability (Article 33(4) PCT)

The subject matter of claims 1 - 26 is considered industrially applicable. Hence, it meets requirements of Article 33(1) and (4) PCT.

Re Item VIII

Certain observations on the international application

1) The claim numbering is not correct (see claims 13 and claims 14). In order to establish this preliminary opinion "first claim 13" is referred to as claim 11 and "first claim 14" is referred to as claim 12 in the present opinion.

2) Claims should not refer to "paragraphs", but to claims.